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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,211	02/21/2007	Hozumi Tanaka	21581-00491-US	3346

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EXAMINER	
SCHLIENTZ, NATHAN W	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,211	TANAKA ET AL.	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :7/20/06, 10/10/06, 5/8/08, 5/14/08 and 9/18/09.

DETAILED ACTION

Status of the Claims

Claims 1-23 are pending in the present application and are thus examined herein on the merits for patentability. No claim is allowed at this time.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 2 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2 and 15 recite the limitation "the sum of an oxidized coenzyme Q and the reduced coenzyme Q" in the 2nd and 3rd lines. There is insufficient antecedent basis for this limitation in the claim. The claims recite a proportion of the reduced coenzyme Q to the sum of oxidized coenzyme Q and reduced coenzyme Q, but claims 1 and 14 do not recite anything about oxidized coenzyme Q or the sum of oxidized and reduced coenzyme Q.

2. Claims 9 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 is dependent from claim 1, and claim 21 is dependent from claim 14, neither of which explicitly recite an antioxidant. However,

claims 9 and 21 list suitable antioxidants. It is not clear if claim 9 was intended to depend from claim 8 which recites that the composition of claim further contains an antioxidant. With regard to claim 21, it is not clear if Applicant intended to state that an antioxidant is included in the method of claim 14, and said antioxidant is selected from the group consisting of those listed in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1, 4-10, 12-14 and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gers-Barlag et al. (US 2003/0003122) in view of Fuji '962 (EP 1 440 962), Fuji '445 (WO 03/033445; the English language equivalent US 7,364,751 is referred to herein), Uda et al. (US 5,486,508), and Lutka et al. (Acta Poloniae Pharmaceutica, 1997)

Determination of the scope and content of the prior art

(MPEP 2141.01)

Gers-Barlag et al. teach Pickering emulsions comprising an oil phase, a water phase, at least one cyclodextrin, and emulsifiers (Abstract). Gers-Barlag et al. further teach that in particular, Pickering emulsions according to their invention can also contain antioxidants ([0100]). The antioxidants are selected from a group which includes ubiquinone (coenzyme Q_{10}) and ubiquinol (reduced coenzyme Q_{10}) ([0101]). Gers-Barlag et al. further teach that α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin are suitable for use in their invention, with β-cyclodextrin and γ-cyclodextrin being particularly preferred ([0046]-[0051]). Gers-Barlag et al. further teach that the cyclodextrin is present at less than 10.0% by weight, preferably between 0.1 and 5.0% by weight of the total preparation ([0051]), and the one or more antioxidant(s) is/are present at 0.001 to 30% by weight, preferably 0.05-20% by weight, in particular 1-10% by weight of the total preparation ([0102]). Gers-Barlag et al. also teach that other suitable antioxidants include lycopene, glutathione, cysteine, citric acid, vitamin C and vitamin E ([0101]).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Gers-Barlag et al. do not explicitly disclose emulsions comprising cyclodextrin, ubiquinol and water, as instantly claimed. However, it was known at the time of the invention that reduced coenzyme Q_{10} is susceptible to oxidation and thus unstable, and that cyclodextrins are useful for improving water-solubility and stability of slightly water-

soluble drugs. Fuji '962 and Fuji '751 teach that reduced coenzyme Q10 itself has antioxidant activity, but it has not been put into practical use because of its drawback that it is susceptible to oxidation and thus unstable (col. 2, ln. 24-37 of Fuji '751). Uda et al. teach pharmaceutical compositions comprising a slightly water-soluble drug, a cyclodextrin and a water-soluble organic solvent (Abstract). Uda et al. teach adding cyclodextrin dissolved in water to a slightly water-soluble drug dissolved in a water-soluble organic solvent followed by evaporating and distilling off the water-soluble organic solvent and water to obtain a powdered composition. In many cases the composition thus obtained forms an inclusion compound with the cyclodextrin (col. 1, ln. 48-59). Uda et al. teach that the water-solubility is 3 to 50 times higher than that of compositions obtained by conventional techniques, and an unstable drug can be stabilized (col. 1, ln. 59 to col. 2, ln. 14). Also, Lutka et al. teach that addition of cyclodextrin to coenzyme Q_{10} decelerated the degradation of the coenzyme (Abstract).

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of the invention to combine ubiquinol with the cyclodextrin and water, according to Gers-Barlag et al., in order to increase the solubility and stability of the ubiquinol, as reasonably taught by Uda et al. and Lutka et al. It would also have been *prima facie* obvious for one of ordinary skill in the art to include more than one antioxidant, such as lycopene, glutathione, cysteine, citric acid, vitamin C and vitamin E, as reasonably taught by Gers-Barlag et al.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

4. Claims 1-4, 6, 7, 10-16, 18-20, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuji et al. (WO 02/092067; the English language equivalent US 2004/0115181 is referred to herein).

Determination of the scope and content of the prior art

(MPEP 2141.01)

Fuji et al. teach compositions comprising oxidized coenzyme Q and/or reduced coenzyme Q, wherein the coenzyme has 1 to 12 side chain repeat units (i.e. n = an integer from 1 to 12), preferably 10 side chain repeat units, oxidized coenzyme Q_{10} and reduced coenzyme Q_{10} (Abstract; [0015] and [0016]). When the composition contains both oxidized coenzyme Q and reduced coenzyme Q, the content of reduced coenzyme Q of the whole of oxidized coenzyme Q and reduced coenzyme Q preferably exceeds 20% by weight, and is more preferably 40% by weight or more ([0018]). Fuji et al. teach nose drop formulations comprising the coenzyme Q and formulation additives, including bases for powder administration such as β-cyclodextrin, dimethyl-β-cyclodextrin, and the like ([0021]).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Fuji et al. do not explicitly disclose a nose drop formulation comprising reduced coenzyme Q, cyclodextrin and water, as instantly claimed. However, Fuji et al. clearly teach that for nose drop formulations examples of additives include β-cyclodextrin and dimethyl-β-cyclodextrin.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of the invention to prepare nose drop formulations comprising oxidized coenzyme Q and/or reduced coenzyme Q, β-cyclodextrin or dimethyl-β-cyclodextrin, and saline, as reasonably taught by Fuji et al. With regard to the proportion of cyclodextrin to reduced coenzyme Q, one of ordinary skill in the art would readily be able to determine the necessary amount of formulation additive to add for a nose drop formulation.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is 571-272-9924. The examiner can normally be reached on 8:30 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NWS

/John Pak/
Primary Examiner, Art Unit 1616